

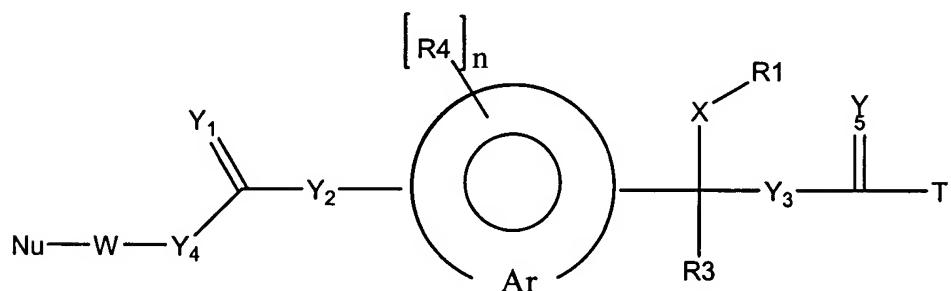
Amendments to and listing of the claims:

Please cancel claims 4-39, 41-73, 75 and 77-87 and amend claims 74, 76 and 88, without prejudice, as shown below in the following listing of all claims ever presented. The following listing of claims replaces all prior versions thereof.

1. (Original) A polymeric cascade prodrug comprising:

- an amine containing biologically active moiety;
- a masking group having at least one nucleophile and being distinct from the carrier.

2. (Original) The prodrug of claim 1 or corresponding polymeric cascade prodrug linker reagent having the following structure:



wherein

T is D or A

D being a residue of an amine containing biologically active moiety and

A being a leaving group;

X is a spacer moiety such as R5-Y6

Y1, Y2 can each be either O, S, or NR6, independently of each other,

Y3, Y5 can each be either O or S, independently of each other,

Y₄ is O, NR₆, or -C(R₇)(R₈)-

Y₆ is O, S, NR₆, succinimide, maleimide, unsaturated carbon-carbon bonds or any heteratom containing a free electron pair or is absent

R₃ is selected from hydrogen, substituted or non-substituted linear, branched or cyclical alkyl or heteroalkyl, aryls, substituted aryls, substituted or non-substituted heteroaryls, cyano, nitro, halogen, carboxy, carboxyalkyl, alkylcarbonyl, or carboxamidoalkyl;

R₄ is selected independently from hydrogen, substituted or non-substituted linear, branched or cyclical alkyl or heteroalkyl, aryl, substituted aryl, substituted or non-substituted heteroaryl, substituted or non-substituted linear, branched, or cyclical alkoxy, substituted or non-substituted linear, branched, or cyclical heteroalkyloxy, aryloxy, or heteroaryloxy, cyano, halogen;

R₅ is selected from substituted or non-substituted linear, branched or cyclical alkyl or heteroalkyl, aryls, substituted aryls, substituted or non-substituted heteroaryls;

R₇ and R₈ are selected from hydrogen, substituted or non-substituted linear, branched or cyclical alkyl or heteroalkyl, aryls, substituted aryls. substituted or non-substituted heteroaryls. carboxyalkyl, alkylcarbonyl, carboxamidoalkyl, cyano, or halogen;

R₆ is selected from hydrogen, substituted or non-substituted linear, branched or cyclical alkyl or heteroalkyl, aryls, substituted aryls, substituted or non-substituted heteroaryls;

R₁ is a polymer;

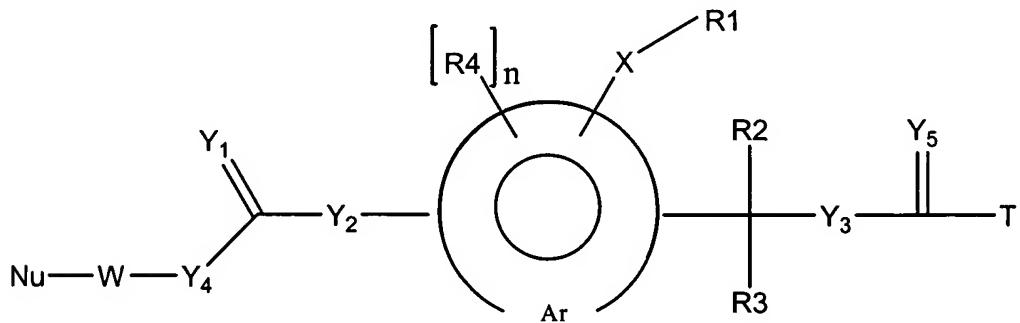
W is selected from substituted or non-substituted linear, branched or cyclical alkyl, aryls, substituted aryls, substituted or non-substituted linear, branched or cyclical heteroalkyl, substituted or non-substituted heteroaryls;

Nu is a nucleophile;

n is zero or a positive integer; and

Ar is a multi-substituted aromatic hydrocarbon or a multi-substituted aromatic heterocycle.

3. (Original) The prodrug of claim 1 or corresponding polymeric cascade prodrug linker reagent having the following structure:



wherein

T is D or A

D being a residue of an amine containing biologically active molecule and

A being a leaving group;

X is a spacer moiety such as R5-Y₆

Y₁, Y₂ can each be either O, S, or NR₆, independently of each other,

Y₃, Y₅ can each be either O or S, independently of each other

Y₄ is O, NR₆, or -C(R₇)(R₈)-

Y₆ is O, S, NR₆, succinimide, maleimide, unsaturated carbon-carbon bonds or any heteratom

containing a free electron pair or is absent,

R₂ and R₃ are selected independently from hydrogen, substituted or non-substituted linear, branched or cyclical alkyl or heteroalkyl, aryls, substituted aryls, substituted or non-substituted heteroaryls, cyano, nitro, halogen carboxy, carboxyalkyl, alkylcarbonyl, or carboxamidoalkyl;

R4 is selected independently from hydrogen, substituted or non-substituted linear, branched or cyclical alkyl or heteroalkyl, aryl, substituted aryl, substituted or non-substituted heteroaryl, substituted or non-substituted linear, branched, or cyclical alkoxy, substituted or non-substituted linear, branched, or cyclical heteroalkyloxy, aryloxy or heteroaryloxy, cyano, halogen;

R5 is selected from substituted or non-substituted linear, branched or cyclical alkyl or heteroalkyl, aryls, substituted aryls, substituted or non-substituted heteroaryls;

R7 and R8 are selected from hydrogen, substituted or non-substituted linear, branched or cyclical alkyl or heteroalkyl, aryls, substituted aryls, substituted or non-substituted heteroaryls, carboxyalkyl, alkylcarbonyl, carboxamidoalkyl, cyano, or halogen;

R6 is selected from hydrogen, substituted or non-substituted linear, branched or cyclical alkyl or heteroalkyl, aryls, substituted aryls, substituted or non-substituted heteroaryls;

R1 is a polymer;

W is selected from substituted or non-substituted linear, branched or cyclical alkyl, aryls, substituted aryls, substituted or non-substituted linear, branched or cyclical heteroalkyl, substituted or non-substituted heteroaryls;

Nu is a nucleophile;

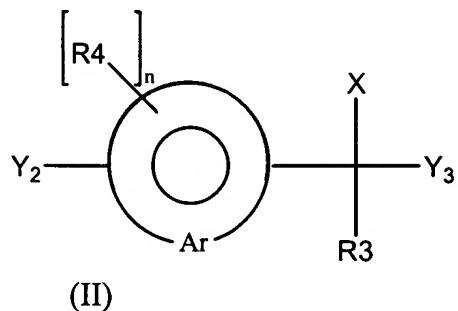
n is zero or a positive integer; and

Ar is a multi-substituted aromatic hydrocarbon or a multi-substituted aromatic heterocycle.

4-39. (Canceled)

40. (Original) Method for the synthesis of a polymeric prodrug comprising:

- providing a starting molecule of Formula II



- synthesizing at least one intermediate compound from the starting molecule of Formula II; and

- attaching an amine-containing biologically active moiety D to the at least one intermediate compound to form the polymeric prodrug;

wherein

Y₂ is selected from O, S, or NR₆

Y₃ is selected from O or S

X is a spacer moiety such as R₅-Y₆;

R₃ is selected independently from hydrogen, substituted or non-substituted linear, branched or cyclical alkyl or heteroalkyl, aryl, substituted aryl, substituted or non-substituted heteroaryl, cyano, nitro, halogen, carboxy, carboxyalkyl, alkylcarbonyl or carboxamidoalkyl;

R₄ is selected from hydrogen, substituted or non-substituted linear, branched or cyclical alkyl or heteroalkyl, aryl, substituted aryl, substituted or non-substituted heteroaryl, substituted or non-substituted linear, branched, or cyclical alkoxy, substituted or non-substituted linear, branched, or cyclical heteroalkyloxy, aryloxy or heteroaryloxy, cyano, or halogen; R₁ is selected from substituted or non-substituted linear, branched or cyclical alkyl or heteroalkyl, aryls, substituted aryls, substituted or non-substituted heteroaryls;

R6 is selected from hydrogen, substituted or non-substituted linear, branched or cyclical alkyl or heteroalkyl, aryl, substituted aryl substituted or non-substituted heteroaryl; and

Y₆ is O, S, NR₆, succinimide, maleimide, unsaturated carbon-carbon bonds or a heteroatom containing a free electron pair;

n is zero or a positive integer and

Ar is a multi-substituted aromatic hydrocarbon or a multi-substituted aromatic heterocycle.

41-73. (Canceled)

74. (Currently Amended) A method for hydrolysing the prodrug of ~~any one of~~ claims 1 to 36 claim 1 comprising a step of placing the prodrug in solution with a pH of approximately 7.4.

75. (Canceled)

76. (Currently Amended) Method of administration of an amine-containing moiety to a living organism comprising:

- a first step of providing a polymeric cascade prodrug according to ~~any one of claims 1 to 39~~ claim 1;
- a second step of administering the polymeric cascade prodrug to the living organism; and
- a third step of cleaving the amine-containing moiety from the polymeric cascade prodrug by means of a substantially non-enzymatic reaction.

77-87. (Canceled)

88. (Currently Amended) A method of providing a therapeutically useful

concentration of a biologically active molecule by *in vivo* cleavage of the biologically active molecule from the prodrug according to ~~any one of claims 1 to 39~~ claim 1.